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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,792	11/10/2005	Giuseppe Pier Pelicci	LEDER-0014	4653

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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11/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,792	PELICCI ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-23 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-23 are all the pending claims subject to lack of unity restriction.

2. The preliminary amendment of 3/30/05 to correct the improper claim dependency has been considered and entered.

3. It is noted that Claims 11 and 20-23 are "use" claims and are not drawn to statutory subject matter under 35 U.S.C. 101. Based on a most reasonable interpretation of the claims, the claims have been construed as a method or process and analyzed for unity of invention below. Applicants are required to cancel the claims or amend the claims to recite statutory subject matter in their reply to this Office Action.

Lack of Unity: Restriction

4. Restriction is required under 35 U.S.C. 121 and 372.

The claims of the present application relate to anti-acetylated histone antibodies and their use in a method for determining whether to administer or continue administering a HDAC inhibitor in a treatment for a disorder.

In assessing whether the requirements of unity of invention of an application are met, identification of the technical features that each solution to a technical problem contributes over the prior art (special technical features) must be made. If then a technical relationship between the solutions, involving one or more of the same technical features, can be recognized, the requirements of unity of invention are said to be met.

The method of detecting histone acetylation in a sample derived from the tissue effected by a disorder where treatment of the disorder with an HDAC has been started/ is continued using an anti-acetylated histone antibody was already known before the priority date of the present application. For example, Butler et al. (Clin. Can. Res. 7:962-970 (2001); cited in the IDS of 3/30/05) describes on p. 965, Col. 1, ¶ 3 that MEL cells incubated with pyroxamide showed accumulated histone acetylation (Figure 2B) measured in Western Blot using polyclonal antibodies against acetylated histones H2A, H2B, H3 or H4, and on p. 966, Col. 2, ¶1, CWR22 tumors excised from mice treated with pyroxamide showed increased accumulated acetylation of histone (Figure 6A) by Western blot. Marks et al. (Nature Reviews Cancer 1:194-202 (2001); cited in the IDS of 3/30/05) describes on p. 197, Col. 2, last ¶ the occurrence of histone acetylation after HDAC treatment in normal and tumor cells and accumulation of acetylated histone is a useful marker of HDAC biological activity and can be used to monitor dosing in clinical trials (p. 199, Col. 2, ¶3).

As no technical features can be distinguished which, in light of the prior art, could be regarded as special technical features on which a unifying concept could be based, there is no single inventive concept underlying the plurality of claimed inventions.

5. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The resulting separate inventions, as presently identified, have been grouped according to the order in which they have been claimed.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-11, drawn to a method for determining whether an HDAC inhibitor should started, continued or not in treating a disorder comprising measuring histone acetylation with an antibody recognizing acetyled histone in a sample and comparing the histone acetylation to a reference sample, a method of determining whether treatment with an HDAC inhibitor is to be started, continued or not, and/or the classification of tumors based on antibody binding to acetylated histone.

Group II, claim(s) 12-19, drawn to an antibody for binding peptides of SEQ ID NO: 4 and 5, but not 2, 6, 10 and 11, or an antibody for binding peptodes of SEQ ID NO: 4, 5 and 6, but not 2, or an antibody produced by hybridomas G2M-T25 or G2M-T52, or a hybridoma G2M-T25 or G2M-T52, or a diagnostic kit for measuring histone acetylation levels with an anti-histone acetylation antibody where the kit comprises the T25 or T52 antibody.

Group III, claim(s) 20-23, drawn to a method of targeting a T25- or T52- antibody conjugated to a substance to hyperacetylation sites.

6. Two different methods are presented in Groups I and III. The methods do not share similar steps and have a similar outcome or endpoint. The method of Group I involves in a sample from a disorder the level of histone acetylaiton with an anti-histone acetylation antibody in order to determine whether an HDAC inhibitor should be started or continued or not based on the level of the histone acetylation. The method of Group III involves targeting an anti-histone antibody conjugated to a therapeutic or diagnostic substance to sites with hyperacetylation of histones. The inventions are not similar or overlapping and raise different issues for patentability.

7. The product of Group II and the methods of Groups I and III are related as product and process of using. Otherwise, the methods of Groups I and III are not required to be practiced with an anti-histone acetylation antibody where a different

reagent such as fluorescein-labeled octapeptides which are substrates for HDAC (Hoffmann et al. (Bioconjug. Chem. 2001 Jan-Feb;12(1):51-5)).

8. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

10. This application contains claims directed to the following patentably distinct species (disorder):

a) diseases in which the induction of hyperacetylation of histones has a beneficial effect resulting in differentiation and/or apoptosis of a patient's tumor cells

b) diseases that show aberrant recruitment of HDAC activity

c) conditions associated with abnormal gene expression

d) autoimmune diseases

e) proliferative diseases

The species are independent or distinct because even though the species are broad in scope, the disorders falling within each would not all share a common feature or function that any other species would necessarily share. For example, an autoimmune disease is generally expected to involve a non-self tolerant immune response whereas proliferative diseases would not require an autoimmune component.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-5 and 8-11 are generic.

11. This application contains claims directed to the following patentably distinct nested species (disorder- cancer):

skin cancer, melanoma, estrogen receptor-dependent and independent breast cancer, ovarian cancer, testosteron receptor-dependent and independent prostate cancer, renal cancer, colon and colorectal cancer, pancreatic cancer, bladder cancer,

esophageal cancer, stomach cancer, genitourinary cancer, gastrointestinal cancer, uterine cancer, astrocytomas, gliomas, basal cancer and squameous cell carcinoma, sarcomas as Kaposi's sarcoma and osteosarcoma, head and neck cancer, small cell and non-small cell lung carcinoma, leukemia, lymphomas and other blood cell cancers, and thyroid resistance syndrome.

The species are independent or distinct because the species of cancer can originate from any number of different cell types (e.g., epithelial, mesothelial or endothelial) and are under the influence of different growth factors, hormones, cytokines, etc. Additionally, numerous studies have shown that antigen density and affinity for different biomolecules is highly variable amongst different tissues and organs, in addition to there being differences to the extent to which biomolecules are able to penetrate tissues and organs.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-5 and 8-11 are generic.

12. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SUPERVISORY PATENT EXAMINER